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PATENTS
Attorney Docket No.: BD1 CIP FWC IV

#54
B. K. Denny
6/19/97

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) : Sherie L. Morrison, et al.
Serial No. : 08/266,154
Filed : June 27, 1994
For : RECEPTORS BY DNA SPLICING AND
EXPRESSION
Group Art Unit : 1806
Examiner : Julie E. Reeves, Ph.D.

Palo Alto, California
June 11, 1997

Honorable Assistant Commissioner
of Patents
Washington, D.C. 20231

DECLARATION OF SHERIE L. MORRISON
PURSUANT TO 37 C.F.R. § 1.132

I, SHERIE L. MORRISON, declare that:

1. I am a co-inventor in the above-identified patent application.
2. I have reviewed the May 15, 1996 Declaration of Marc J. Shulman,
including its exhibits, that is attached at Tab A.

3. Nothing in that declaration describes our invention in such full, clear, concise, and exact terms as to enable any person skilled in the art to make and use our invention.

4. Specifically, the letter comprising Exhibit A to that declaration identifies the major project of a graduate student working with Dr. Shulman, Gabrielle Boulianne, but contains no detail as to the method used in that project.

5. Exhibit B to that declaration is a copy of a research proposal describing the "desirability of chimeric antibodies." The proposal states:

"My aim in this project has been to take advantage of the available technology in our laboratory to assay for the expression of functional antibody by chimeric mouse/human immunoglobulin genes. In this way, I can test *whether variable region genes can be transposed to various constant region genes while maintaining functional activity....If these constructions produce functional antibody*, this technique could then be applied to generate chimeric antibodies of any antigenic specificity. It will *then* be possible to test *whether* this method provides a general source of specific antibody useful in therapy." (emphasis added.)

The additional disclosure in this proposal does not enable one of skill in the art to practice our invention because it does not contain a full, clear, concise and exact description of co-transfection and co-expression of exogenous antibody chain genes. The two examples in the proposal describe the use of cell lines which produce an endogenous antibody chain which is assembled together with the exogenous chain to form the antibody. While Dr. Shulman states in his declaration that "a method for expressing both genes in the same cell had been developed by Drs. Ochi and Hozumi and communicated to me", the proposal specifically states that this was a "personal communication" and does not describe the method. The proposal contains none of the specifics of vector design or expression system.

6. Exhibit C to that declaration constitutes a report sent to the Arthritis Society dated September 1983. One paragraph of that report describes work on chimeric antibodies and in that paragraph Dr. Shulman states:

"We have begun to test whether the chimeric gene encoding such immunoglobulin can in fact function and whether the antigen binding specificity of the chimeric immunoglobulin is the same as for the original mouse immunoglobulin.... Currently we are testing the function of the chimeric κ gene."

No specifics concerning DNA cloning, vector construction, transfection, or expression systems is given that would enable someone skilled in the art to practice the claimed invention.

7. Exhibit D to that declaration is a copy of an abstract that Dr. Shulman states was published in conjunction with a symposium held from October 2-6, 1983 in Ontario, Canada. That abstract describes what work was done by Dr. Shulman and his colleagues; but it does not explain how the work was done, again omitting specifics concerning DNA cloning, vector construction, and transfection methods that would enable someone skilled in the art to practice the claimed invention.

8. The May 15, 1996 declaration also attaches an earlier declaration and associated exhibits executed by Dr. Shulman on May 21, 1994. Exhibit C to the 1994 declaration constitutes a January 19, 1983 letter from Dr. Shulman to the Johns Hopkins University School of Medicine outlining Dr. Shulman's proposal for the subject matter of his upcoming lecture. Dr. Shulman states:

"In my presentation I propose to discuss how one might combine the hybridoma system with recombinant DNA and in vitro mutagenesis techniques to generate antibodies where the variable and constant regions are precisely specified. This approach to antibody specificity

looks good on paper. *My reservations about its feasibility* stem from the facts that (sic) on the one hand our knowledge about V region structure and C region function is rather incomplete, and on the other hand the technical difficulties in altering antibodies are great." (emphasis added.)

9. Dr. Shulman states that Exhibit D to the 1994 declaration constitutes copies of some of the slides which accompanied the lecture discussed in the January 19 letter. Those slides do not enable one skilled in the art to practice the claimed invention for several reasons. First, they do not explain how to clone the exogenous DNA coding for the antibody heavy or light chains or how to assemble that DNA into a functional expression vector. Second, the slide labelled "Construction and Expression of an Ig Heavy Chain Gene" looks similar to textbook diagrams showing normal VDJ assembly and isotype switching. That slide provides no information about how to make the recombinant gene. In addition, there is no slide showing "Construction and Expression", or any other information, specific to the light chain gene. Finally, on the slide labelled "Engineering the V Region", M13 is identified as a possible vector for the immunoglobulin gene. That vector has no eukaryotic selectable markers and therefore is inappropriate for use in a eukaryotic expression system.

10. I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that all these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both under

By Shene L. Morrison

Dated: June 11, 1997

1990-1991		1991-1992		1992-1993		1993-1994		1994-1995		1995-1996		1996-1997		1997-1998		1998-1999		1999-2000		2000-2001		2001-2002		2002-2003		2003-2004		2004-2005		2005-2006		2006-2007		2007-2008		2008-2009		2009-2010		2010-2011		2011-2012		2012-2013		2013-2014		2014-2015		2015-2016		2016-2017		2017-2018		2018-2019		2019-2020		2020-2021		2021-2022		2022-2023		2023-2024		2024-2025		2025-2026		2026-2027		2027-2028		2028-2029		2029-2030		2030-2031		2031-2032		2032-2033		2033-2034		2034-2035		2035-2036		2036-2037		2037-2038		2038-2039		2039-2040		2040-2041		2041-2042		2042-2043		2043-2044		2044-2045		2045-2046		2046-2047		2047-2048		2048-2049		2049-2050		2050-2051		2051-2052		2052-2053		2053-2054		2054-2055		2055-2056		2056-2057		2057-2058		2058-2059		2059-2060		2060-2061		2061-2062		2062-2063		2063-2064		2064-2065		2065-2066		2066-2067		2067-2068		2068-2069		2069-2070		2070-2071		2071-2072		2072-2073		2073-2074		2074-2075		2075-2076		2076-2077		2077-2078		2078-2079		2079-2080		2080-2081		2081-2082		2082-2083		2083-2084		2084-2085		2085-2086		2086-2087		2087-2088		2088-2089		2089-2090		2090-2091		2091-2092		2092-2093		2093-2094		2094-2095		2095-2096		2096-2097		2097-2098		2098-2099		2099-2100		2100-2101		2101-2102		2102-2103		2103-2104		2104-2105		2105-2106		2106-2107		2107-2108		2108-2109		2109-2110		2110-2111		2111-2112		2112-2113		2113-2114		2114-2115		2115-2116		2116-2117		2117-2118		2118-2119		2119-2120		2120-2121		2121-2122		2122-2123		2123-2124		2124-2125		2125-2126		2126-2127		2127-2128		2128-2129		2129-2130		2130-2131		2131-2132		2132-2133		2133-2134		2134-2135		2135-2136		2136-2137		2137-2138		2138-2139		2139-2140		2140-2141		2141-2142		2142-2143		2143-2144		2144-2145		2145-2146		2146-2147		2147-2148		2148-2149		2149-2150		2150-2151		2151-2152		2152-2153		2153-2154		2154-2155		2155-2156		2156-2157		2157-2158		2158-2159		2159-2160		2160-2161		2161-2162		2162-2163		2163-2164		2164-2165		2165-2166		2166-2167		2167-2168		2168-2169		2169-2170		2170-2171		2171-2172		2172-2173		2173-2174		2174-2175		2175-2176		2176-2177		2177-2178		2178-2179		2179-2180		2180-2181		2181-2182		2182-2183		2183-2184		2184-2185		2185-2186		2186-2187		2187-2188		2188-2189		2189-2190		2190-2191		2191-2192		2192-2193		2193-2194		2194-2195		2195-2196		2196-2197		2197-2198		2198-2199		2199-2200		2200-2201		2201-2202		2202-2203		2203-2204		2204-2205		2205-2206		2206-2207		2207-2208		2208-2209		2209-2210		2210-2211		2211-2212		2212-2213		2213-2214		2214-2215		2215-2216		2216-2217	
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For Other Than A Small Entity

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Examination Procedure
Examining Group 1806

Docket No. BD1 CIP FWC IV

Applicant(s) : Sherie L. Morrison, et al.
Serial No. : 08/266,154
Filed : June 27, 1994
For : RECEPTORS BY DNA SPLICING
AND EXPRESSION
Group Art Unit : 1806
Examiner : Julie E. Reeves, Ph.D.

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GROUP 1800

Hon. Assistant Commissioner
for Patents
Washington, D.C. 20231

Palo Alto, California
June 11, 1997

TRANSMITTAL LETTER

Sir:

Transmitted herewith: ☐ a Preliminary Amendment;
☒ a Response to Examiner's Action; ☐ a Supplemental
Amendment; ☐ a substitute Specification; ☒ a Declaration;
☐ a Supplemental Declaration; ☐ a Power of Attorney;
☐ an Associate Power of Attorney; ☐ formal drawings; to be
filed in the above-identified patent application.

FEE FOR ADDITIONAL CLAIMS

☒ A fee for additional claims is not required.

☐ A fee for additional claims is required.

The additional fee has been calculated as shown below:

	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR		PRESENT EXTRA		RATE		ADDITIONAL FEES
TOTAL CLAIMS	30	-	48	* =	0	X	\$22 =		\$0
INDEPENDENT CLAIMS	3	-	6	** =	0	X	\$80 =		\$0
FIRST PRESENTATION OF A MULTIPLE DEPENDENT CLAIM							+ \$260 =		\$0

* If less than 20, insert 20.

TOTAL \$0

** If less than 3, insert 3.

[] A check in the amount of \$_____ in payment of the filing fee is transmitted herewith.

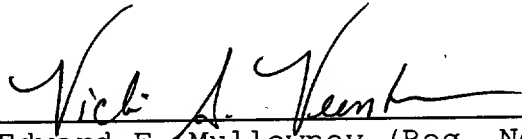
[X] The Commissioner is hereby authorized to charge payment of any additional filing fees required under 37 C.F.R. § 1.16, in connection with the paper(s) transmitted herewith, or credit any overpayment of same, to deposit Account No. 06-1075. A duplicate copy of this transmittal letter is transmitted herewith.

[] Please charge \$_____ to Deposit Account No. 06-1075 in payment of the filing fee. A duplicate copy of this transmittal letter is transmitted herewith.

EXTENSION FEE

[X] The following extension is applicable to the Response filed herewith; [] \$110.00 extension fee for response within first month pursuant to 37 C.F.R. § 1.17(a); [] \$390.00 extension fee for response within second month pursuant to 37 C.F.R. § 1.17(b); [X] \$930.00 extension fee for response within third month pursuant to 37 C.F.R. § 1.17(c); [] \$1,470.00 extension fee for response within fourth month pursuant to 37 C.F.R. § 1.17(d).

- [X] A check in the amount of [] \$110.00; [] \$390.00;
[X] \$930.00; [] \$1,470.00; in payment of the
extension fee is transmitted herewith.
- [X] The Commissioner is hereby authorized to charge
payment of any additional fees required under
37 C.F.R. § 1.17 in connection with the paper(s)
transmitted herewith, or to credit any overpayment
of same, to Deposit Account No. 06-1075. A
duplicate copy of this transmittal letter is
transmitted herewith.
- [] Please charge the [] \$110.00; [] \$390.00;
[] \$930.00; [] \$1,470.00; extension fee to Deposit
Account No. 06-1075. A duplicate copy of this
transmittal letter is transmitted herewith.



Edward F. Mullenney (Reg. No. 27,459)
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on June 11, 1997

Vicki S. Veenker
Name of Person Signing Certificate


Signature of Person Signing Certificate

June 11, 1997
Date of Signature